CLAIMS

What is claimed is:

1. A method of treating, preventing, modifying or managing pain, which comprises administering to a patient in need of such treatment, prevention, modification or management a therapeutically or prophylactically effective amount of a selective cytokine inhibitory drug, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof.

2. The method of claim 1, which further comprises administering to the patient a therapeutically or prophylactically effective amount of at least one second active agent.

3. The method of claim 2, wherein the second active agent is capable of relieving or reducing pain.

4. The method of claim 2, wherein the second active agent is an antidepressant, antihypertensive, anxiolytic, calcium channel blocker, alpha-adrenergic receptor agonist, alpha-adrenergic receptor antagonist, ketamine, anesthetic, muscle relaxant, non-narcotic analgesic, opioid analgesic, anti-inflammatory agent, immunomodulatory agent, immunosuppressive agent, corticosteroid, anticonvulsant, cox-2 inhibitor, hyperbaric oxygen, or a combination thereof.

5. The method of claim 2, wherein the second active agent is salicylic acid acetate, celecoxib, ketamine, gabapentin, carbamazepine, oxcarbazepine, phenytoin, sodium valproate, prednisone, nifedipine, clonidine, oxycodone, meperidine, morphine sulfate, hydromorphone, fentanyl, acetaminophen, ibuprofen, naproxen sodium, griseofulvin, amitriptyline, imipramine or doxepin.

6. The method of claim 1, wherein the pain is nociceptive pain or neuropathic pain.

7. The method of claim 6, wherein the pain is associated with chemical or thermal burn, cut of the skin, contusion of the skin, osteoarthritis, rheumatoid arthritis, tendonitis, or myofascial pain

8. The method of claim 6, wherein the pain is diabetic neuropathy, post herpetic neuralgia, trigeminal neuralgia, post-stroke pain, complex regional pain syndrome,

sympathetic maintained pain syndrome, reflex sympathetic dystrophy, reflex neurovascular dystrophy, reflex dystrophy, spinal cord injury pain, Sudeck atrophy of bone, algoneurodystrophy, shoulder hand syndrome, post-traumatic dystrophy, cancer related pain, phantom limb pain, fibromyalgia, chronic fatigue syndrome, radiculopathy, luetic neuropathy, or painful neuropathic condition induced from a drug.

9. The method of claim 8, wherein the complex regional pain syndrome is type I or type II.

10. The method of claim 8, wherein the painful neuropathic condition is iatrogenically induced by vincristine, velcade or thalidomide.

11. The method of claim 1, wherein the pain is visceral pain, migraine, tension-type headache, post-operative pain, or mixed pain of nociceptive and neuropathic pain.

12. The method of claim 1, wherein the stereoisomer of the selective cytokine inhibitory drug is enantiomerically pure.

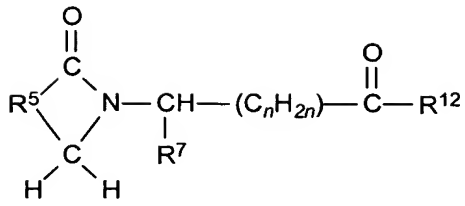
13. The method of claim 1, wherein the selective cytokine inhibitory drug is 3-(3,4-dimethoxy-phenyl)-3-(1-oxo-1,3-dihydro-isoindol-2-yl)-propionamide.

14. The method of claim 13, wherein the selective cytokine inhibitory drug is enantiomerically pure.

15. The method of claim 1, wherein the selective cytokine inhibitory drug is cyclopropanecarboxylic acid {2-[1-(3-ethoxy-4-methoxy-phenyl)-2-methanesulfonyl-ethyl]-3-oxo-2,3-dihydro-1 *H*-isoindol-4-yl}-amide.

16. The method of claim 15, wherein the selective cytokine inhibitory drug is enantiomerically pure.

17. The method of claim 1, wherein the selective cytokine inhibitory drug is of formula (I):



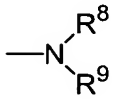
(I)

wherein n has a value of 1, 2, or 3;

R^5 is o-phenylene, unsubstituted or substituted with 1 to 4 substituents each selected independently from the group consisting of nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, hydroxy, amino, alkylamino, dialkylamino, acylamino, alkyl of 1 to 10 carbon atoms, alkyl of 1 to 10 carbon atoms, and halo;

R^7 is (i) phenyl or phenyl substituted with one or more substituents each selected independently of the other from the group consisting of nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, hydroxy, amino, alkyl of 1 to 10 carbon atoms, alkoxy of 1 to 10 carbon atoms, and halo, (ii) benzyl unsubstituted or substituted with 1 to 3 substituents selected from the group consisting of nitro, cyano, trifluoromethyl, carbothoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, hydroxy, amino, alkyl of 1 to 10 carbon atoms, alkoxy of 1 to 10 carbon atoms, and halo, (iii) naphthyl, and (iv) benzyloxy;

R^{12} is -OH, alkoxy of 1 to 12 carbon atoms, or

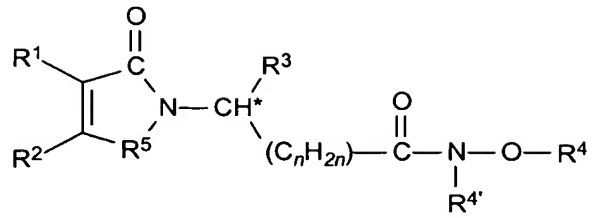


R^8 is hydrogen or alkyl of 1 to 10 carbon atoms; and

R^9 is hydrogen, alkyl of 1 to 10 carbon atoms, $-COR^{10}$, or $-SO_2R^{10}$, wherein R^{10} is hydrogen, alkyl of 1 to 10 carbon atoms, or phenyl.

18. The method of claim 17, wherein the selective cytokine inhibitory drug is enantiomerically pure.

19. The method of claim 1, wherein the selective cytokine inhibitory drug is of formula (II):



(II)

wherein each of R^1 and R^2, when taken independently of each other, is hydrogen, lower alkyl, or R^1 and R^2, when taken together with the depicted carbon atoms to which each is bound, is *o*-phenylene, *o*-naphthylene, or cyclohexene-1,2-diyl, unsubstituted or substituted with 1 to 4 substituents each selected independently from the group consisting of nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, hydroxy, amino, alkylamino, dialkylamino, acylamino, alkyl of 1 to 10 carbon atoms, alkoxy of 1 to 10 carbon atoms, and halo;

R^3 is phenyl substituted with from one to four substituents selected from the group consisting of nitro, cyano, trifluoromethyl, carbethoxy, carbomethoxy, carbopropoxy, acetyl, carbamoyl, acetoxy, carboxy, hydroxy, amino, alkyl of 1 to 10 carbon atoms, alkoxy of 1 to 10 carbon atoms, alkylthio of 1 to 10 carbon atoms, benzyloxy, cycloalkoxy of 3 to 6 carbon atoms, C_4-C_6-cycloalkylidenemethyl, C_3-C_{10}-alkylidenemethyl, indanyloxy, and halo;

R^4 is hydrogen, alkyl of 1 to 6 carbon atoms, phenyl, or benzyl;

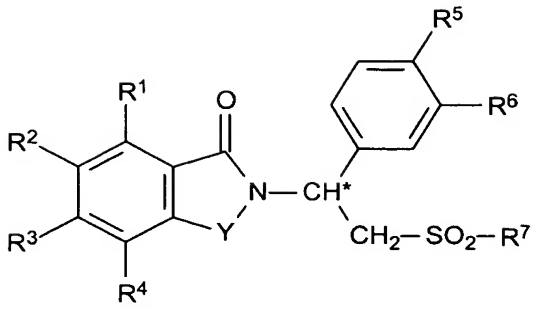
$R^{4'}$ is hydrogen or alkyl of 1 to 6 carbon atoms;

R^5 is $-CH_2-$, $-CH_2-CO-$,$-SO_2-$,-S-, or -NHCO-; and

n has a value of 0, 1, or 2.

20. The method of claim 19, wherein the selective cytokine inhibitory drug is enantiomerically pure.

21. The method of claim 1, wherein the selective cytokine inhibitory drug is of formula (III):



(III)

wherein the carbon atom designated * constitutes a center of chirality;

Y is C=O, CH2, SO_2, or $CH_2C=O$;

each of R^1, R^2, R^3, and R^4, independently of the others, is hydrogen, halo, alkyl of 1 to 4 carbon atoms, alkoxy of 1 to 4 carbon atoms, nitro, cyano, hydroxy, or $-NR^8R^9$; or any two of R^1, R^2, R^3, and R^4 on adjacent carbon atoms, together with the depicted phenylene ring are naphthylidene;

each of R^5 and R^6, independently of the other, is hydrogen, alkyl of 1 to 4 carbon atoms, alkoxy of 1 to 4 carbon atoms, cyano, or cycloalkoxy of up to 18 carbon atoms;

R^7 is hydroxy, alkyl of 1 to 8 carbon atoms, phenyl, benzyl, or $NR^{8'}R^{9'}$;

each of R^8 and R^9 taken independently of the other is hydrogen, alkyl of 1 to 8 carbon atoms, phenyl, or benzyl, or one of R^8 and R^9 is hydrogen and the other is $-COR^{10}$ or $-SO_2R^{10}$, or R^8 and R^9 taken together are tetramethylene, pentamethylene, hexamethylene, or $-CH_2CH_2X^1CH_2CH_2-$ in which X^1 is -O-, -S- or -NH-; and

each of $R^{8'}$ and $R^{9'}$ taken independently of the other is hydrogen, alkyl of 1 to 8 carbon atoms, phenyl, or benzyl, or one of $R^{8'}$ and $R^{9'}$ is hydrogen and the other is $-COR^{10'}$ or $-SO_2R^{10'}$, or $R^{8'}$ and $R^{9'}$ taken together are tetramethylene, pentamethylene, hexamethylene, or $-CH_2CH_2X^2CH_2CH_2-$ in which X^2 is -O-, -S-, or -NH-.

22. The method of claim 21, wherein the selective cytokine inhibitory drug is enantiomerically pure.

23. A method of treating, preventing, modifying or managing pain, which comprises administering to a patient in need of such treatment, prevention, modification or management a therapeutically or prophylactically effective amount of a selective cytokine inhibitory drug, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, before, during or after surgery, psychological or physical therapy directed at reducing or avoiding a symptom of pain in the patient.

24. A pharmaceutical composition comprising a selective cytokine inhibitory drug, or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof, and a second active agent capable of relieving or reducing pain.

25. The pharmaceutical composition of claim 24, wherein the second active agent is an antidepressant, antihypertensive, anxiolytic, calcium channel blocker, alpha-adrenergic receptor agonist, alpha-adrenergic receptor antagonist, ketamine, anesthetic, muscle relaxant, non-narcotic analgesic, opioid analgesic, anti-inflammatory agent, immunomodulatory agent, immunosuppressive agent, corticosteroid, anticonvulsant, cox-2 inhibitor, hyperbaric oxygen, or a combination thereof.

26. The pharmaceutical composition of claim 24, wherein the second active agent is salicylic acid acetate, celecoxib, ketamine, gabapentin, carbamazepine, oxcarbazepine, phenytoin, sodium valproate, prednisone, nifedipine, clonidine, oxycodone, meperidine, morphine sulfate, hydromorphone, fentanyl, acetaminophen, ibuprofen, naproxen sodium, griseofulvin, amitriptyline, imipramine or doxepin.